

From the INTERNATIONAL BUREAU

## PCT

NOTIFICATION CONCERNING  
TRANSMITTAL OF COPY OF INTERNATIONAL  
PRELIMINARY REPORT ON PATENTABILITY  
(CHAPTER I OF THE PATENT COOPERATION  
TREATY)  
(PCT Rule 44bis.1(c))

To:

BOWERSOX, Leonard, D.  
Kilyk & Bowersox, P.L.L.C.  
3603-E Chain Bridge Road  
Fairfax, VA 22030  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)  
27 July 2006 (27.07.2006)

Applicant's or agent's file reference  
5010-234-PCT

## IMPORTANT NOTICE

International application No.  
PCT/US2005/001031

International filing date (day/month/year)  
12 January 2005 (12.01.2005)

Priority date (day/month/year)  
12 January 2004 (12.01.2004)

Applicant

APPLERA CORPORATION et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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INTERNATIONAL BUREAU

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 5010-234-PCT	<b>FOR FURTHER ACTION</b>	
	See item 4 below	
International application No. PCT/US2005/001031	International filing date ( <i>day/month/year</i> ) 12 January 2005 (12.01.2005)	Priority date ( <i>day/month/year</i> ) 12 January 2004 (12.01.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant APPLERA CORPORATION		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I Basis of the report
<input type="checkbox"/>	Box No. II Priority
<input type="checkbox"/>	Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input checked="" type="checkbox"/>	Box No. IV Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI Certain documents cited
<input checked="" type="checkbox"/>	Box No. VII Certain defects in the international application
<input checked="" type="checkbox"/>	Box No. VIII Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).

Date of issuance of this report  
17 July 2006 (17.07.2006)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Yolaine Cussac  e-mail: pt11@wipo.int
Facsimile No. +41 22 338 82 70	

To:

see form PCT/ISA/220

4/8

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

FOR FURTHER ACTION  
See paragraph 2 below

International application No.  
PCT/US2005/001031

International filing date (day/month/year)  
12.01.2005

Priority date (day/month/year)  
12.01.2004

International Patent Classification (IPC) or both national classification and IPC  
B01L3/00, C12Q1/68

Applicant  
APPLERA CORPORATION

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized Officer

Marti, P

Telephone No. +49 89 2399-7858



**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
 a sequence listing  
 table(s) related to the sequence listing
  - b. format of material:  
 in written format  
 in computer readable form
  - c. time of filing/furnishing:  
 contained in the international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.
3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**Box No. IV Lack of unity of invention**

1.  In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
  - paid additional fees.
  - paid additional fees under protest.
  - not paid additional fees.
2.  This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is:
  - complied with
  - not complied with for the following reasons:

see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
  - all parts.
  - the parts relating to claims Nos.

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	7-13,23,24,26-28
	No: Claims	1-8,14-22,25,29-35
Inventive step (IS)	Yes: Claims	
	No: Claims	1-35
Industrial applicability (IA)	Yes: Claims	1-35
	No: Claims	

2. Citations and explanations

see separate sheet

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

see separate sheet

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item IV

**Lack of unity of invention**

1. The present set of claims comprises the following groups of subject-matter:

Group A Claims 1-15: Assay device comprising an optically transparent cover and a substrate with at least one sample receiving chamber, a distributor channel, at least one reaction chamber and at least one vent, wherein the substrate comprises at least a portion adjacent the reaction chamber which has a thermal conductivity of 0.25 W/m<sup>2</sup>K or greater.

Group B Claims 16-29: Method comprising introducing a liquid sample into one or more sample receiving chambers of an assay device, moving the liquid sample into a plurality of reaction chambers covered by an optically transparent cover, venting gas from the reaction chambers through a venting system, and increasing the temperature of the liquid sample in the plurality of reaction chambers at a rate of one °C/second or greater.

Group C Claims 30-35: Method comprising introducing a liquid containing a nucleic acid sequence into one or more sample receiving chambers of an assay device, moving the liquid sample with capillary force into a plurality of reaction chambers covered by an optically transparent cover, venting gas from the reaction chambers through a venting system, and amplifying at least a portion of the nucleic acid sequence in the reaction chambers.

The common inventive concept linking together all groups is a device comprising an optically transparent cover and a substrate with at least one sample receiving chamber, a distributor channel and at least one reaction chamber and at least one vent. Since this concept is not novel, the different subject-matters are not so linked as to form a single inventive concept.

Therefore, the requirements of Rule 13 PCT are not fulfilled. See also Item VIII, point 3 below.

**Re Item VIII**

**Certain observations on the international application**

1. Claim 1 does not define that the liquid sample is transported through the distributor channel by capillary force. However, this is an essential feature of the invention (Art. 6 PCT). Note that the whole application does not provide any support for other transport means than capillary force.  
The same applies to claim 16.
2. Claim 16 does not define that the reaction chamber should have a thermal conductivity of 0.25 W/m<sup>2</sup>K or greater. However, this is an essential feature in order to heat the reaction chamber at a high rate (Art. 6 PCT).  
The same applies to claim 30.
3. Although claims 16 and 30 have been drafted as separate independent claims, they relate effectively to the same subject-matter and differ from each other only with regard to the definition of the subject-matter. Therefore, these claims lack conciseness (Art. 6 PCT).
4. The term "about" in claims 1, 3-6, 13, 16-18, 20, and 33 is vague and undefined, resulting in lack of clarity (Art. 6 PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

1. Reference is made to the following documents:

- D1: EP-B-1 062 042
- D2: WO 03/019158 A
- D3: US 2003/138941 A1
- D4: WO 03/089139 A
- D5: US 2002/094303 A1

2.1 Document D1, cited in the application, discloses an assay device (10) comprising an optically transparent cover (= "Deckelkörper" or "Abdeckfolie", 16) and a substrate (= Grundplatte, 12) with at least one sample receiving chamber (= Probenaufnahmekammer, 20), a distributor channel (24), at least one reaction chamber (28) and at least one vent (3). Further, D1 mentions in col. 10, line 35 that the substrate can be made of silicon (= Silizium), i.e. a material which has a thermal conductivity above 5 W/m<sup>°</sup>K.

Hence, the subject-matter of claim 1 lacks novelty over D1 (Art. 33.2 PCT).

2.2 D2 discloses an assay device comprising an optically transparent cover (= Deckfläche, see page 4) and a substrate (= Probenkammermatrix, 1) with at least one sample receiving chamber (3), a distributor channel (4), at least one reaction chamber (2) and at least one vent (= Öffnung zum Entlüften, see page 8). Further, also D2 mentions in claim 11 that the substrate can comprise a layer of silicon or a silicon containing compound.

The device is used for amplifying nucleic acid sequences (PCR).

Therefore, D2 is novelty destroying for the subject-matter of claims 1 and 30 (Art. 33.2 PCT).

2.3 D3 discloses an assay device (100) comprising an optically transparent cover (= sealing layer, 40) and a substrate (36) with at least one sample receiving chamber (6), a distributor channel (30), at least one reaction chamber (26) and at least one vent (24). Metallic powder filling is used in order to provide for improved conduction of heat (see paragraph 82), the same as in the present application.

The device is utilised for fluorescence-based assay, such as PCR.

Therefore, the subject-matter of claims 1 and 30 lacks novelty over D3 (Art. 33.2 PCT).

2.4 D5 discloses a method comprising introducing a liquid sample into one or more sample receiving chambers (24-1, 24-2, 24-3) of an assay device (reactor), moving the liquid sample into a plurality of reaction chambers (24a, see also figure 11b)

covered by an optically transparent cover (14), venting gas from the reaction chambers through a venting system (24-4), and increasing the temperature of the liquid sample in the plurality of reaction chambers at a rate of 20 °C/second (see paragraph 97).

Hence, the subject-matter of claim 16 lacks novelty over D5 (Art. 33.2 PCT).

3. If claim 1 were amended to define that the substrate comprises a first material and a thermally conductive filler, then the subject-matter of claim 1 could be considered as novel over D1. The objective technical problem to be solved by a such amended claim 1 can be seen in the provision of an alternative material having high thermal conductivity.

However, assay devices comprising a first material and a thermally conductive filler are already known in the art, for example from D4.

A skilled person being aware of D1 and looking for a way to solve the above mentioned problem would obviously consider the teaching of D4 in order to arrive at the claimed solution.

Therefore, an accordingly amended claim 1 would not involve an inventive step in the light of D1 in combination with D4 (Art. 33.3 PCT).

4. Dependent claims 2-15, 17-29 and 31-35 contain features which either are disclosed in the cited documents or fall within the customary practice followed by persons skilled in the art and do not involve an inventive step as no particular or unexpected effect is apparent.

**Re Item VII**

**Certain defects in the international application**

1. The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

**PCT/US2005/001031**

## INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/US2005/001031A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 B01L3/00 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 B01L C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 062 042 B (MICROPARTS GESELLSCHAFT FUER MIKROSTRUKTURTECHNIK MBH; MERLIN GESELLSC) 28 May 2003 (2003-05-28) cited in the application the whole document	1-8, 14, 15
Y	-----	9-15, 27, 28, 31
X	WO 03/019158 A (BESTMANN, LUKAS; DUAL, JUERG; BAECHI, DANIEL) 6 March 2003 (2003-03-06)	1-8, 16-22, 25, 29, 30, 32-35
Y	page 6 - page 12; figure 1 -----	26-28, 31, 35 -/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

## Date of the actual completion of the international search

22 June 2005

## Date of mailing of the international search report

30/06/2005

## Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

## Authorized officer

Martí, P

## INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/US2005/001031

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/138941 A1 (GONG HAIQING ET AL) 24 July 2003 (2003-07-24)  paragraph '0082! paragraph '0105! - paragraph '0106! paragraph '0118! - paragraph '0120!; figure 1 -----	1-8,14, 15, 30-32, 34,35
Y	WO 03/089139 A (COOL OPTIONS, INC) 30 October 2003 (2003-10-30) paragraph '0017! - paragraph '0019! paragraph '0023! - paragraph '0037! -----	9-15,26, 35
X	US 2002/094303 A1 (YAMAMOTO TAKATOKI ET AL) 18 July 2002 (2002-07-18) paragraph '0094! - paragraph '0099!; figures 1c,3,11b -----	16-23, 30-33
X	US 5 498 392 A (WILDING ET AL) 12 March 1996 (1996-03-12) the whole document -----	30
A	US 2003/152994 A1 (WOUDENBERG TIMOTHY W ET AL) 14 August 2003 (2003-08-14) the whole document -----	

## INTERNAL SEARCH REPORT

Information on patent family members

Inte  
nal Application No  
PCT/US2005/001031

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 1062042	B	27-12-2000	DE AT AU AU BR CA DE WO EP ES HK IL JP	19810499 A1 241430 T 739563 B2 3034099 A 9909249 A 2323424 A1 59905743 D1 9946045 A1 1062042 A1 2203093 T3 1035683 A1 138286 A 2002505946 T	16-09-1999 15-06-2003 18-10-2001 27-09-1999 28-11-2000 16-09-1999 03-07-2003 16-09-1999 27-12-2000 01-04-2004 10-10-2003 19-02-2004 26-02-2002
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## INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l Application No  
PCT/US2005/001031

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5498392	A	CA 2134476 A1 CA 2134477 A1 CA 2134478 A1 DE 69303483 D1 DE 69303483 T2 DE 69303898 D1 DE 69303898 T2 DE 69312483 D1 DE 69312483 T2 DE 69319427 D1 DE 69319427 T2 DE 69322774 D1 DE 69322774 T2 EP 0637996 A1 EP 0637997 A1 EP 0639223 A1 EP 0637998 A1 EP 0637999 A1 ES 2106341 T3 ES 2127276 T3 GR 3025037 T3 GR 3029509 T3 HK 16897 A HK 1001305 A1 JP 3298882 B2 JP 7506430 T JP 7506431 T	11-11-1993 11-11-1993 11-11-1993 08-08-1996 06-02-1997 05-09-1996 20-02-1997 04-09-1997 12-02-1998 06-08-1998 10-12-1998 04-02-1999 17-06-1999 15-02-1995 15-02-1995 22-02-1995 15-02-1995 15-02-1995 01-11-1997 16-04-1999 30-01-1998 28-05-1999 13-02-1997 16-11-2001 08-07-2002 13-07-1995 13-07-1995
US 2003152994	A1 14-08-2003	US 6825047 B1 US 6124138 A US 6126899 A AU 706862 B2 AU 2604897 A CA 2250212 A1 DE 69700499 D1 DE 69700499 T2 EP 0889751 A1 JP 2000508528 T WO 9736681 A1	30-11-2004 26-09-2000 03-10-2000 24-06-1999 22-10-1997 09-10-1997 14-10-1999 23-03-2000 13-01-1999 11-07-2000 09-10-1997